

1    WHAT IS CLAIMED IS:

1                   1.       A transgenic knockout mouse whose genome comprises a disruption in  
2   the mouse's endogenous melanopsin gene, wherein the disruption prevents the expression of a  
3   functional melanopsin protein in cells of the mouse.

1                   2.       The transgenic knockout mouse of claim 1, wherein the mouse  
2   comprises a homozygous disruption of the melanopsin gene.

1                   3.       The method of claim 1, the homozygous disruption results in the  
2   transgenic knockout mouse exhibiting an attenuated circadian rhythm phase-shift in response  
3   to a light pulse during a dark portion of an environmental dark/light cycle.

1                   4.       A cell isolated from the transgenic knockout mouse of claim 1,  
2   wherein the genome of the cell comprises a disruption in its endogenous melanopsin gene,  
3   and wherein the homozygous disruption prevents the expression of a functional melanopsin  
4   protein in said cell.

1                   5.       A method for identifying a therapeutic agent for modulating circadian  
2   rhythm in a mammal, the method comprising:  
3                   administering an agent to a transgenic knockout animal whose genome  
4   comprises a disruption in its endogenous melanopsin gene, wherein the disruption prevents  
5   the expression of a functional melanopsin protein in cells of the animal and the animal  
6   comprises a homozygous disruption of the melanopsin gene; and  
7                   selecting an agent that modulates the regulation of circadian rhythm in the  
8   animal.

1                   6.       The method of claim 5, wherein the knockout animal displays an  
2   attenuated circadian rhythm phase-shift response to a light pulse during a dark portion of an  
3   environmental dark/light cycle.

1                   7.       The method of claim 5, wherein the selecting step comprises selecting  
2   an agent that enhances the animal's circadian rhythm phase-shift response to a light pulse  
3   during a dark portion of an environmental dark/light cycle.

- 1                    8.        The method of claim 5, wherein the animal is a mouse.
- 1                    9.        A method of modulating circadian rhythm in a mammal in need  
2 thereof, the method comprising administering to the mammal an effective amount of the  
3 agent selected in claim 5.
- 1                    10.       The method of claim 9, wherein timing of administration of the  
2 selected agent is pre-determined to coincide with an appropriate phase of an existing  
3 circadian rhythm to produce a selected modulation of the circadian rhythm.
- 1                    11.       The method of claim 9, wherein the selected agent is used to treat or  
2 prevent a sleep disorder.
- 1                    12.       The method of claim 9, wherein the mammal has a condition selected  
2 from the group selected from insomnia, Seasonal Affective Disorder, Shift Work  
3 dysrhythmia, delayed-sleep phase syndrome, and jet-lag.
- 1                    13.       The method of claim 9, wherein the mammal is a human.
- 1                    14.       The method of claim 9, wherein the selected agent is administered in  
2 conjunction with melatonin or a compound that suppresses or stimulates melatonin  
3 production.
- 1                    15.       The method of claim 9, wherein the selected agent is administered in  
2 conjunction with light therapy.
- 1                    16.       A method of modulating circadian rhythm in a mammal in need  
2 thereof, the method comprising administering to the mammal an effective amount of a  
3 melanopsin modulator.
- 1                    17.       The method of claim 16, wherein timing of administration of the  
2 modulator is pre-determined to coincide with an appropriate phase of an existing circadian  
3 rhythm to produce a selected modulation of the circadian rhythm.
- 1                    18.       The method of claim 16, wherein the modulator is used to treat or  
2 prevent a sleep disorder.

1                    19.     The method of claim 16, wherein the mammal has a condition selected  
2     from the group selected from insomnia, Seasonal Affective Disorder, Shift Work  
3     dysrhythmia, delayed-sleep phase syndrome, and jet-lag.

1                    20.     The method of claim 16, wherein the mammal is a human.

1                    21.     The method of claim 16, wherein the modulator is administered in  
2     conjunction with melatonin or a compound that suppresses or stimulates melatonin  
3     production.